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Proximity Effects. XXXV. Stereospecific Synthesis and Acetolysis of *cis*- and *trans*-5-Methylcyclooctyl Tosylates[1a,b]

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cis- and *trans*-5-methylcyclooctanol were synthesized by routes which allow unambiguous assignment of configuration, and their *p*-toluenesulfonates were solvolyzed in glacial acetic acid–sodium acetate. Product analysis suggests that the *cis* isomer **2a** reacted almost completely by a transannular path, while the *trans* isomer **2b** underwent mainly normal elimination and substitution. Mechanistic implications of the data are discussed.

A study of the formolysis of deuterium-labeled *cis*-cyclooctene oxide[2] has established the predominance of 1,5- over 1,3-hydride shift and has confirmed the stereospecific nature of the reaction. The present work was undertaken to determine the effect of placing a methyl group, with its electron-donating yet relatively small "conformation-fixing" properties, in the 5-position of a cyclooctane ring relative to a leaving group. The 5-hydrogen atom in the *cis* isomer **2a** is *trans* to the leaving group, and a direct concerted 1,5-shift is possible. A 1,5-shift in the *trans* isomer **2b**, however, would have to proceed through a carbonium ion.

Recently Allinger and Greenberg[3] have reported the acetolysis of the 5-*t*-butylcyclooctyl tosylates. Assignments of configuration to the corresponding alcohols were based on the composition of the olefin mixtures from the acetolyses and were supported by n.m.r. studies and by infrared analysis of the reduction products of 5-*t*-butylcyclooctanone. Similar considerations in the case of the 5-methylcyclooctanols did not permit unambiguous assignments of configuration.

5-Methylcyclooctanone was prepared as described previously[4] except that 3-methyl-1,5-diiodopentane was used instead of the corresponding dibromide in the alkylation reaction with acetonitrile; this modification gave higher yields of the dinitrile. 5-Methylcyclooctanone was reduced by seven different procedures to mixtures of the alcohols **1**. The results are summarized in Table I. The configurational assignments are based on a stereospecific synthesis of the *cis* isomer which will be described presently.

TABLE I

REDUCTIONS OF 5-METHYLCYCLOOCTANONE

Reduction	*cis*-5-Methylcyclooctanol[a]	*trans*-5-Methylcyclooctanol[a]
$LiAlH_4/Et_2O$	68.5	31.5
Na/wet Et_2O	56.5	43.5
$H_2/Pt/HOAc$	63.5	36.5
$Al(i\text{-}PrO)_3$ (equil.)	47	53
$NaBH_4/MeOH$	67	33
$LiAl(O\text{-}t\text{-}Bu)_3H$	64	36
H_2/Ni, high pressure	53	47

[a] Percentages of the alcohols (which were not separable by gas chromatography) were determined by gas chromatography of the corresponding acetate mixtures. Because of the closeness of the separation, maximum error is estimated at ±5%.

It can be seen that the isomers are of about equal thermodynamic stability, in contrast to the 4-methylcyclohexanols[5] and the 5-*t*-butylcyclooctanols.[3,6]

Nuclear magnetic resonance has been used frequently to distinguish between axial and equatorial protons in the cyclohexane series.[7] Allinger and Greenberg, by "fixing" the conformation of the cyclooctane ring with a *t*-butyl group, found support for their configurational assignments by a similar difference in chemical shift between axial and equatorial protons. Conformational mobility in the 5-methylcyclooctanols does not permit configurational assignments by n.m.r.; indeed the values found for the C-1 protons (τ = 6.24 for the *cis* isomer and τ = 6.37 for the *trans* isomer) are the reverse of what one would predict assuming fixed conformations. The most striking difference in the two spectra is found in the methylene region; in the *trans* isomer the absorption is sharp, while in the *cis* isomer it is broad and diffuse. This suggests that the ring protons of the *trans* isomer are "flipping" faster (Fig. 1) than those of the *cis* isomer and therefore appear to be more equivalent. We have observed this phenomenon in two other cases.[8,9]

cis-5-Methylcyclooctanol was synthesized stereospecifically by the scheme outlined in Fig. 2. Bicyclo[3.3.1]nonan-9-one (**7**) could be prepared in one step from 1-bromobicyclo[3.3.1]nonan-9-one[10] (**3**) by hydrogenolysis over a palladium-on-calcium carbonate catalyst. However, the sequence developed by Woodward and Foote starting with compound **4** was the method of choice for obtaining large quantities of the ketone.[11] A modified Baeyer–Villiger oxidation of **7** gave the lactone **8** in good yield. Lithium aluminum hydride reduction of **8** to the glycol **9** followed by monotosylation and lithium aluminum hydride reduction gave *cis*-5-methylcyclooctanol (**1a**), identical in all respects with one of the alcohols obtained by reduction of 5-methylcyclooctanone and different from the other.[12] Treatment of its tosylate **2a** with tetraethylammonium ace-

(1) (a) Supported in part by a research grant (NSF-G5055) of the National Science Foundation. (b) Paper XXXIV: *J. Am. Chem. Soc.*, **85**, 3601 (1963). (c) National Institutes of Health Predoctoral Fellow, 1961–1963; National Science Foundation Summer Fellow, 1961.

(2) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *J. Am. Chem. Soc.*, **82**, 6366 (1960).

(3) N. L. Allinger and S. Greenberg, *ibid.*, **84**, 2394 (1962).

(4) A. C. Cope and G. L. Woo, *ibid.*, **85**, 3601 (1963).

(5) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *ibid.*, **78**, 2579 (1956). The ratio of isomers at equilibrium was found to be 12/88 *cis*/*trans*.

(6) The ratio of isomers at equilibrium was found to be 64/36 *cis*/*trans*.[3]

(7) H. L. Lewin and S. Winstein, *J. Am. Chem. Soc.*, **84**, 2464 (1962), and references cited therein.

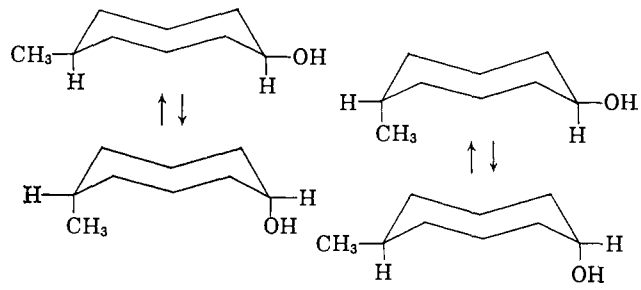
(8) The methylene regions of *cis*- and *trans*-5-phenylcyclooctanol are very nearly identical with those of the respective 5-methylcyclooctanols (A. C. Cope and R. B. Kinnel, to be published).

(9) *cis*-Cyclooctene presents a sharper methylene absorption than the *trans* isomer and therefore appears to be less rigid (unpublished observation of T. V. Van Auken).

(10) A. C. Cope and M. E. Synerholm, *J. Am. Chem. Soc.*, **72**, 5228 (1950).

(11) Analytical data and physical constants for compound **6** may be found in C. S. Foote, Ph.D. Thesis, Harvard University, 1961, while the analytical data and physical constants for compounds **4** and **5** are described in D. M. Gale, Ph.D. Thesis, Massachusetts Institute of Technology, 1963. Detailed experimental procedures for the conversion of **4** to **7** may be found in either thesis. Ketone **7** has been prepared by a third route [D. M. Bailey, J. E. Bowers, and C. D. Gutsche, *J. Org. Chem.*, **28**, 610 (1963)]. Footnote 16 of this reference describes infrared and mixture melting point comparisons with a sample of the ketone prepared by the Woodward–Foote method which establish identity of the two samples.

(12) The samples for these comparisons were obtained by lithium aluminum hydride reduction of the acetates after separation by gas chromatography.



cis-5-Methylcyclooctanol (1a) *trans*-5-Methylcyclooctanol (1b)

Figure 1.

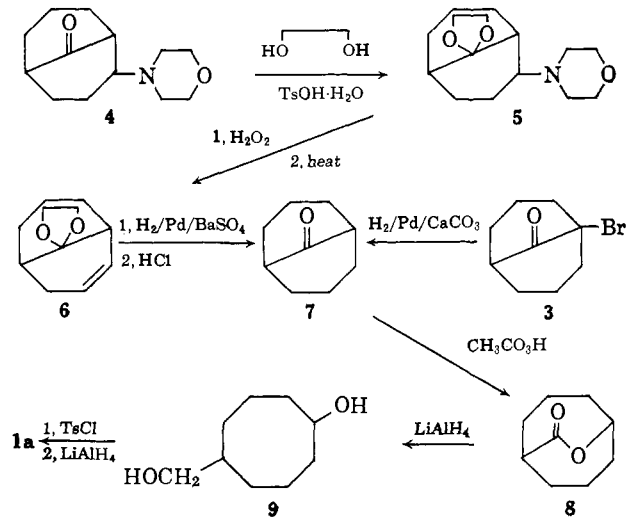


Figure 2.

tate gave the *trans*-acetate which was reduced with lithium aluminum hydride to alcohol **1b**, identical in all respects with the other alcohol from reduction of 5-methylcyclooctanone. Thus the configurations of the 5-methylcyclooctanols were unambiguously established.

Results and Discussion

cis- and *trans*-5-methylcyclooctyl tosylates were prepared and each was solvolyzed in glacial acetic acid–0.5 *M* sodium acetate for 1 day at room temperature, followed by heating at about 45° for 16 to 24 hr. The *cis*-tosylate **2a** gave, after reduction of the solvolysis products with lithium aluminum hydride, 84.3% of 1-methylcyclooctene (**10**),[13] 9.7% of 5-methylcyclooctene (**11**),[4] 5.5% of 1-methylcyclooctanol (**12**),[13] and 0.5% of a mixture which was mainly **1b**. The *trans*-tosylate after reduction gave 8.2% of **10**, 74.0% of **11**, 1.2% of **12**,[14] 4.6% of **1b**, and 10.1% of **1a**.[15] The products were identified by their retention times on one or more columns and by comparison of their infrared spectra with those of authentic samples. 3-Methylcyclooctene,[4] 4-methylcyclooctene,[4] and the 2- and 3-methylcyclooctanols[4] were eliminated as possible products in either solvolysis. The olefin and acetate products, with the exception of 1-methylcyclooctyl acetate (**15**),[16] which decomposes somewhat to **10**, were shown to be stable to the reaction conditions. When either *cis*- or *trans*-5-methylcyclooctanol was subjected to the reaction conditions, acetylation took place only to the extent of 9%.

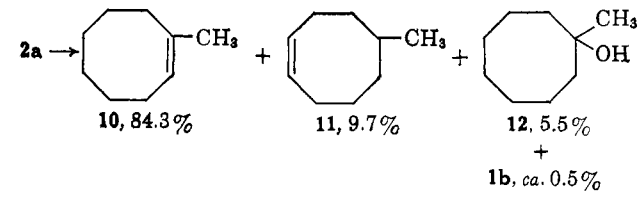
It is worthy of note that the normal elimination (olefin **11**) and substitution (alcohol **1b**) products constitute only about 10% of the products from the *cis* isomer.

(13) A. C. Cope and H. C. Campbell, *J. Am. Chem. Soc.*, **74**, 179 (1952).

(14) H. C. Brown and M. Borkowski, *ibid.*, **74**, 1894 (1952).

(15) The remainder (1.9%) contained two or more components and was not investigated.

(16) A sample of this acetate was kindly provided by Dr. R. C. Petterson.



2b → 10 (8.2%) + 11 (74%) + 12 (1.2%) + 1b (4.6%) + 1a (10.1%) + (1.9%) unidentified

Figure 3.

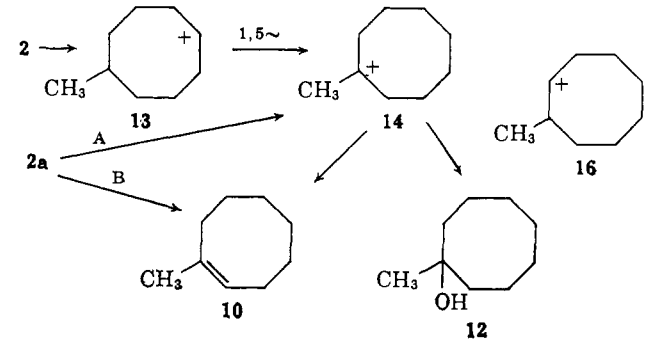


Figure 4.

Migration of a hydride ion from the 5-position to form the more stable tertiary carbonium ion **14**, which could lose a proton to form **10** or react with solvent to give **12** would account for the major course of the reaction. It is also possible that olefin **10** and carbonium ion **14** are formed directly by concerted processes (paths A and B). The intermediacy of **16** (from a 1,4-hydride shift) which could rearrange to **14** or give **10** directly seems unlikely since neither 3-methylcyclooctene nor the 2-methylcyclooctanols were found as products. (Furthermore, a 1,4-hydride shift has not been observed previously in these systems.) The olefins **10** and **11** were recovered unchanged when subjected separately to the reaction conditions. Thus, the acetolysis of *cis*-5-methylcyclooctyl tosylate can be explained either in terms of concerted or carbonium ion mechanisms, but at least the partial intervention of the free carbonium ion **14** is suggested.

In the reaction of the *trans*-tosylate **2b**, paths similar to A and B are not available. The main course of the reaction is the formation of the normal elimination (**11**) and substitution (**1a**) products. The 1,5-shift products **12** and **10** can arise only through ion **13**, presumably by rearrangement to **14**. Isolation of *trans*-5-methylcyclooctanol from the acetolysis necessitated the intermediacy of carbonium ion **13**.[17]

That neither the 5-methylcyclooctyl tosylates nor the 5-*t*-butylcyclooctyl tosylates[3] gave rise to detectable amounts of 1,3-hydride shift may be explained either in terms of relative carbonium ion stability or perhaps more likely as a conformational phenomenon. One should note that *cis*-cyclooctene oxide, a system that does give rise to 1,3-shift,[2] differs considerably in ring geometry from any reasonable cyclooctane ring conformation. It may be that the occurrence of a 1,3-shift during the formolysis of *cis*-cyclooctene oxide[2] is the exception rather than the rule for solvolysis of cyclooctane derivatives.

Experimental[18]

3-Methyl-1,5-diiodopentane.—To a mixture of 147 g. of 3-methyl-1,5-pentanediol and 37 g. of red phosphorus, stirred and

(17) The infrared spectrum of the initial tosylate showed no hydroxyl absorption, and no free alcohol was detected in the acetolysis products before lithium aluminum hydride reduction. Therefore the presence of *trans*-alcohol in the acetolysis products after lithium aluminum hydride reduction could not be explained by incomplete tosylation.

(18) Melting points are corrected and boiling points are uncorrected.

cooled in ice, was added 370 g. of iodine during a period of 3.5 hr. The mixture was stirred for 1 hr. at ice-bath temperature and for 10 hr. at 28°. After standing for an additional 4.5 hr. at room temperature, the brown-black paste was heated with stirring at 40–45° for 1.5 hr. and allowed to stand for 24 hr. The mixture was extracted with 3 l. of ether and the ether solution was washed with 2 l. of water, 1 l. of dilute sodium hydroxide, again with 2 l. of water, and dried. The ether was removed by distillation and the residue was distilled through a 45-cm. Vigreux column, yielding 269 g. of 3-methyl-1,5-diiodopentane (63%), b.p. 139–141° (8.5 mm.), $n^{25}D$ 1.5852.

Anal. Calcd. for $C_6H_{12}I_2$: C, 21.32; H, 3.55. Found: C, 21.44; H, 3.63.

5-Methylnonanedinitrile.—Sodium amide[19] was prepared from 24 g. of sodium metal and 500 ml. of liquid ammonia. To this stirred suspension 41 g. of redistilled acetonitrile was added over 10 min., a Dry Ice–acetone bath being used for external cooling. This was followed by dropwise addition (45 min.) of a mixture of 155 g. of 3-methyl-1,5-diiodopentane and 35 g. of acetonitrile. The Dry Ice–acetone bath was removed and stirring continued for 1.5 hr., after which 500 ml. of anhydrous ether was added. The mixture was vented and stirred for 12 hr. The resulting paste was extracted with 500 ml. of ether, and the ether extract was washed with water, dilute hydrochloric acid, saturated sodium carbonate until basic, with water until neutral, and dried (magnesium sulfate). The ether was removed by distillation under reduced pressure and the residue (57 g.) was distilled through a 30-cm. spinning-band column, yielding 39.3 g. (52%) of 5-methylnonanedinitrile, b.p. 117–121° (0.07 mm.), $n^{25}D$ 1.4478; lit.[4] b.p. 115° (0.125 mm.), $n^{25}D$ 1.4483.

Anal.[20] Calcd. for $C_{10}H_{16}N_2$: C, 73.12; H, 9.82; N, 17.06. Found: C, 72.83; H, 9.57; N, 17.32.

***cis*- and *trans*-5-Methylcyclooctanols (1). A. By Lithium Aluminum Hydride Reduction.**—A solution of 208 mg. of 5-methylcyclooctanone[4] in 15 ml. of ether was added dropwise to a stirred suspension of 100 mg. of lithium aluminum hydride in 20 ml. of ether. After 6 hr. of heating at reflux the mixture was decomposed with enough 1 *N* hydrochloric acid to dissolve the hydroxides and was extracted with ether. The combined ether extracts were neutralized with saturated sodium bicarbonate solution and dried over magnesium sulfate. The ether was removed under reduced pressure and the residue (187.5 mg., 90%) was purified by chromatography on alumina (untreated Merck "Special"); the main fraction, eluted with 5% methanol in ether, weighed 117 mg. (56%). Acetylation of this fraction gave a mixture of 63.5% *cis*- and 36.5% *trans*-acetates.[21]

B. By Catalytic Hydrogenation.—A solution of 140 mg. of 5-methylcyclooctanone in 10.5 ml. of glacial acetic acid containing 2 drops of concentrated hydrochloric acid was hydrogenated over 183 mg. of prereduced platinum dioxide. The uptake was 108% of theoretical. The catalyst was removed by filtration after dilution with 50 ml. of water. The filtrate was extracted three times with ether, and the extracts were neutralized with saturated sodium carbonate solution and dried over magnesium sulfate. Acetylation of the residue (156 mg.) after removal of the ether gave a mixture of 63.5% *cis*- and 36.5% *trans*-acetates.[21]

C. By Reduction with Sodium and Wet Ether.—To a solution of 178 mg. of 5-methylcyclooctanone in 5 ml. of ether over 5 ml. of a nearly saturated solution of potassium carbonate was added *ca.* 0.5 g. of small flattened pieces of sodium metal. The reaction was complete in 3 hr., after which 20 ml. of water was added cautiously. The aqueous layer was extracted with ether and the combined ether layers were washed with water and dried over magnesium sulfate. The residue (180 mg.) obtained on removal of the ether was found to contain only the mixture of 5-methylcyclooctanols.[21] Acetylation followed by gas chromatography revealed a composition of 56.5% *cis* and 43.5% *trans*.

D. Reduction with Aluminum Isopropoxide.—A suspension of 241 mg. of 5-methylcyclooctanone, 465 mg. of aluminum isopropoxide, 26 ml. of isopropyl alcohol, and 0.5 ml. of acetone was stirred under reflux in the absence of moisture; 5-ml. samples were taken at 13.5, 48.0, 110.0, 350, and 735 hr. and diluted with 8 ml. of cold 6 *N* hydrochloric acid and extracted three times with ether. In each case, the ether extracts were washed seven times with water, dried over magnesium sulfate, and the ether evaporated to give a mixture of the 5-methylcyclooctanols and some unchanged ketone.[21] The percentage of alcohol present increased from 82.7 to 83.2 to 85.2 to 93.5 to 100% as the reaction proceeded to completion by removal of acetone. The mixtures thus obtained were dissolved in pyridine and treated with 0.5 ml. of acetic anhydride as described below. Analysis by gas chromatography[21] showed the same *cis*/*trans* ratio in each case (47/53), demonstrating that equilibrium had been reached by the time the first sample was taken.

E. By Reduction with Sodium Borohydride.—A solution of 46 mg. of 5-methylcyclooctanone in 10 ml. of methanol was added dropwise to a stirred solution of 61.5 mg. of sodium borohydride in 20 ml. of methanol. The stirred mixture was refluxed for 16 hr. After cooling, a solution of 1.0 g. of sodium hydroxide in 15 ml. of water was added and the mixture was stirred for 2.5 hr. at room temperature, then diluted with an equal volume of water and extracted three times with ether. The combined extracts were washed with saturated ammonium chloride solution until neutral, then with water, and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure gave a residue (34 mg., 72.5%) which consisted of >99% 1.[21] The ratio of isomeric 5-methylcyclooctanols was found to be 67/33 by gas chromatograpic analysis of the acetates.

F. By Reduction with Tri-*t*-butoxy Lithium Aluminum Hydride.—A solution of 234 mg. of anhydrous *t*-butyl alcohol in 20 ml. of ether was added slowly to a stirred solution of 36 mg. of lithium aluminum hydride in 20 ml. of ether. After the mixture had been stirred for 15 min., 43 mg. of 5-*t*-butylcyclooctanone in 20 ml. of ether was added. The suspension was stirred for 21 hr. at 30°, then 20 ml. of 1 *N* hydrochloric acid was added dropwise. The ether layer was separated and the aqueous layer was extracted twice with ether. The combined ether layers were washed twice with water, shaken with magnesium sulfate, and the ether evaporated under reduced pressure. The residue weighed 21.5 mg. (50%), and was shown to contain 57.5% of 5-methylcyclooctanols and 42.5% of 5-methylcyclooctanone. Analysis of the acetates formed from this mixture showed the ratio of alcohols was 64/36 *cis*/*trans*.

G. By Hydrogenation with a Raney Nickel Catalyst.—A solution of 76.5 mg. of 5-methylcyclooctanone in methanol was placed in an autoclave with excess Raney nickel (*ca.* 3 g.) and hydrogenated at 46° under *ca.* 1500 p.s.i. for 19 hr. The suspension was filtered to remove the catalyst, and the solvent was removed under reduced pressure. The residue was taken up in 50 ml. of ether, shaken with Norit and magnesium sulfate, filtered, and the ether evaporated under reduced pressure to a colorless oil (40.3 mg., 52%) which was shown to contain >99% of the 5-methylcyclooctanols. The isomer ratio was 53/47 *cis*/*trans* by the acetate method.

***cis*- and *trans*-5-Methylcyclooctyl Acetates.**—In a typical experiment, 0.5 ml. of acetic anhydride was added to a cooled solution of 69 mg. of the 5-methylcyclooctanols in 6 ml. of dry pyridine. The mixture was allowed to stand at room temperature for 24 hr., then 50 ml. of cold water was added. The mixture was extracted twice with ether and the ether extracts were washed twice with cold 6 *N* hydrochloric acid, once with water, and dried over magnesium sulfate. Removal of the solvent under reduced pressure gave a residue of 91 mg. (101%) which was shown to contain 98.5% of the mixture of acetates.

The *cis* isomer, eluted first from the TCEP column at 127°, had $n^{25}D$ 1.4551.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.40; H, 11.07.

The *trans* isomer had $n^{25}D$ 1.4556.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.70; H, 11.00.

The infrared spectra of the acetates show small but distinct differences.

By experiments with mixtures of the acetates of known concentration the limit of detectability of one isomer in the presence of the other was found to be 2%.[21]

Bicyclo[3.3.1]nonan-9-one (7) from 1-Bromobicyclo[3.3.1]nonan-9-one (3).—A suspension of 67 mg. of 1-bromobicyclo[3.3.1]nonan-9-one,[10] 320 mg. of a 1% palladium-on-calcium carbonate catalyst, and 281 mg. of anhydrous sodium acetate in 15 ml. of absolute ethanol was hydrogenated at 30°. After 40 min. the uptake was 101.5% of the theoretical amount and there was no further uptake. The suspension was filtered and the solid was washed with 15 ml. of ethanol and 20 ml. of pentane. The solution was diluted with 50 ml. of cold water, and the layers were separated. The aqueous layer was extracted three times with pentane. The combined pentane extracts were washed with saturated sodium bicarbonate solution, then three times with water, and dried over magnesium sulfate. Evaporation of the pentane under reduced pressure gave 57.5 mg. of a colorless oil which contained 97% of bicyclo[3.3.1]nonan-9-one by gas chromatographic analysis (TCEP, 150°). A sample of the ketone was collected from the same column.

9-Oxabicyclo[3.3.2]decan-10-one (8).—To a stirred, ice-cooled suspension of 8.0 g. of anhydrous sodium acetate and 22.5 g. of crude **7** (85% pure) in 95 ml. of glacial acetic acid was added

Microanalyses were determined by Dr. S. M. Nagy and associates and by the Scandinavian Microanalytical Laboratories. Methods used for gas chromatography were those described by A. C. Cope and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1647 (1959), ref. 24, with the stationary phases specified here.

(19) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 219.

(20) The analysis was repeated because this sample did not exhibit the bands at 2195 and 1582 cm.$^{-1}$ (probably due to a trace of isonitrile) present in the material reported previously.[4]

(21) Determined by gas chromatography on TCEP at 125°.

dropwise over 40 min. 95 ml. of 40% peracetic acid in acetic acid. The internal temperature was maintained at 5–9° during the addition and the mixture was protected from light with aluminum foil. It was stirred vigorously for 70 min. at 3° and then allowed to come to room temperature and stand for 65 hr. (shorter times led to incomplete reaction). The mixture was poured slowly with swirling and cooling into a suspension of 1 l. of 20% sodium bicarbonate solution, 200 g. of solid sodium bicarbonate, and 500 g. of ice. The resulting solution was extracted three times with ether and the ether extracts were washed twice with an equal volume of brine and dried over magnesium sulfate. Evaporation of the ether gave 20.5 g. (82% yield based on **7** of 85% purity) of the lactone, essentially homogeneous by gas chromatography (silicone grease, 170°). A sample collected from a similar run had m.p. 140.2–143.8° (sealed capillary) and was submitted for analysis. The lactone could also be purified by recrystallization from ether–pentane or by vacuum sublimation.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.18. Found: C, 70.21; H, 9.15.

***cis*-5-Hydroxymethylcyclooctanol (9).**—To a stirred suspension of 5.495 g. of lithium aluminum hydride in 200 ml. of tetrahydrofuran was added over 10 min. with occasional cooling 9.09 g. of **8** in 150 ml. of tetrahydrofuran. The suspension was vigorously stirred at room temperature for 14.5 hr., refluxed for 3 hr., and stirred for 4 additional hr. To it was then added 5.5 ml. of water, 5.5 ml. of 15% sodium hydroxide solution, and 16.5 ml. of water. This suspension was stirred for 17 hr. at room temperature and filtered. The filtrate was dried over magnesium sulfate and the solvent removed under reduced pressure yielding 10.54 g. of oily glycol. The analytical sample, $n^{25}D$ 1.5030, was collected from a silicone grease column at 175°.

Anal. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 67.96; H, 11.50.

A bis-*p*-nitrobenzoate was prepared (white needles from ethyl acetate–ethanol) and melted at 130.5–131.5°.

Anal. Calcd. for $C_{23}H_{24}O_8N_2$: C, 60.52; H, 5.30; N, 6.14. Found: C, 60.32; H, 5.21; N, 6.04.

***cis*-5-Methylcyclooctanol (1a).**—A solution of 677 mg. of crude **9** in 9 ml. of dry pyridine was cooled to 0° and 856 mg. of *p*-toluenesulfonyl chloride in 5 ml. of pyridine was added with swirling. The solution was kept at 2° for 17.3 hr.,[22] when 100 ml. of cold water was added and the product extracted with three portions of methylene chloride. The extracts were washed twice with cold 6 *N* hydrochloric acid, then with cold saturated sodium bicarbonate solution and water. After drying over magnesium sulfate the solvent was removed to give the crude monotosylate (770 mg.). This oil was dissolved in 20 ml. of ether and to it was added 320 mg. of lithium aluminum hydride in 60 ml. of ether. The suspension was stirred at room temperature for 21 hr. and then refluxed for 1 hr. and stirred for 4 additional hr. The excess hydride was decomposed with 30 ml. of 3 *N* hydrochloric acid. An equal volume of water was added, the layers were separated, and the aqueous layer was extracted with two 20-ml. portions of ether. The combined ether layers were washed with cold saturated sodium bicarbonate solution, then with brine, and dried over magnesium sulfate. Evaporation of the ether gave 410 mg. of an oil (73% from the lactone **8**) which was shown to contain about 65% of *cis*-5-methylcyclooctanol by gas chromatographic analysis (silicone grease, 170°).

A 785-mg. sample of the crude alcohol (*ca.* 75% pure) was dissolved in pentane and placed on a column prepared from 30 g. of neutral activity 1 alumina in pentane. The column was washed with 500 ml. of 10% ether in pentane to remove less polar impurities. The alcohol fraction (675 mg.) was eluted with 500 ml. of 10% methanol in ether. A 450-mg. sample of this fraction gave 308 mg. of *cis*-5-methylcyclooctanol when collected on a silicone grease column at 148°. This sample also exhibited only one peak on TCEP at 140°. The analytical sample had $n^{25}D$ 1.4763.

Anal. Calcd. for $C_9H_{18}O$: C, 75.99; H, 12.76. Found: C, 75.95; H, 12.72.

The phenylurethan was prepared, m.p. 56–57° after recrystallization from pentane.

Anal. Calcd. for $C_{16}H_{23}O_2N$: C, 73.53; H, 8.87. Found: C, 73.46; H, 8.73.

***trans*-5-Methylcyclooctanol (1b).**—Crude **2a** (2.02 g.) was prepared (using the procedure described for preparation of the tosylate **2a** for solvolysis) from 1.35 g. of **1a** (about 75% pure) and 2.20 g. of *p*-toluenesulfonyl chloride in 10 ml. of pyridine. The oily tosylate was refluxed with 2 g. of tetraethylammonium acetate monohydrate[23] in 50 ml. of dry acetone for 16 hr. The mixture was allowed to stand for 42 hr. at room temperature after which it was diluted with 250 ml. of ice–water and extracted three times with ether. The ether extracts were washed with cold saturated sodium bicarbonate solution and dried. After removal of the ether under reduced pressure the residue (1.21 g.) was analyzed by gas chromatography (silicone grease, 145°). The major peak, 56% of the area, was *trans*-5-methylcyclooctyl acetate. (A collected sample had a retention time on silicone grease at 145° and TCEP at 122° and an infrared spectrum identical with those of the *trans*-acetate obtained from the alcohol mixture from reduction of 5-methylcyclooctanone.) The crude acetate was dissolved in 50 ml. of dry ether and 160 mg. of lithium aluminum hydride was added. The suspension was stirred at room temperature for 20 hr. Enough 3 *N* hyrochloric acid (*ca.* 20 ml.) was then added to dissolve most of the hydroxides, the layers were separated, and the aqueous layer was extracted with ether. The combined ether layers were washed with cold saturated sodium bicarbonate solution and dried over magnesium sulfate. Evaporation of the ether under reduced pressure gave an oil (917 mg.) which by gas chromatographic analysis (silicone grease, 142°) consisted mainly of **1b**. It was purified as described for **1a**; the alcohol fraction after chromatography weighed 675 mg. and yielded 300 mg. of pure **1b**, $n^{25}D$ 1.4756.

Anal. Calcd. for $C_9H_{18}O$: C, 75.99; H, 12.76. Found: C, 76.20; H, 12.83.

The phenylurethan had m.p. 81.5–82.5° after recrystallization from pentane. The infrared spectra of the phenylurethans showed only minor differences.

Anal. Calcd. for $C_{16}H_{23}O_2N$: C, 73.53; H, 8.87. Found: C, 73.26; H, 8.85.

N.m.r. and Infrared Spectra of the 5-Methylcyclooctanols.—Spectra were obtained in 14% carbon tetrachloride solution at 60 Mc. The alcohol **1a** had absorption at 9.13 τ (doublet, 3 H), J = 5.5 c.p.s., CH_3–; 8.43 τ (center of broad multiplet, 13 H), $-CH_2-$ (12 H) and $CH_3CH <$(1 H); 7.36 τ (singlet, 1 H), >CH–OH; 6.24 τ (broad singlet, 1 H), >CH–OH. Compound **1b** had absorption at 9.14 τ (doublet, 3 H), J 6.0 c.p.s., CH_3–; 8.46 τ (multiplet, 13 H), $-CH_2-$ (12 H) and $CH_3CH <$ (1 H); 7.33 τ (singlet, 1 H), >CH–OH; 6.37 τ (broad singlet, 1 H), >CH–OH.

The infrared spectra of the alcohols in carbon disulfide or carbon tetrachloride were essentially the same except for a moderate band at 970 cm.$^{-1}$ which was present in **1a** and absent in **1b**, and a strong band at 982 cm.$^{-1}$ in **1b** which was nearly absent in **1a**. A one-to-one mixture gave doublets at these frequencies.

Solvolysis of *cis*-5-Methylcyclooctyl *p*-Toluenesulfonate (2a).—A solution of 340 mg. of **1a** in 2.5 ml. of dry pyridine was cooled in a Dry Ice–acetone bath and 700 mg. of *p*-toluenesulfonyl chloride was added. The mixture was kept at about −5° for 62 hr. and then was diluted with 150 ml. of ice–water and extracted three times with ether. The ether extracts were washed at 0° twice with 6 *N* hydrochloric acid and twice with saturated sodium bicarbonate solution and dried at −5° over magnesium sulfate. The solid obtained by removal of the ether under reduced pressure below 0° was recrystallized from pentane at −10°, giving white plates, m.p. 45.0–47.5°, which were solvolyzed immediately.[24] Their weight, 437.5 mg. (63%), was determined by difference when a known weight of solvolysis mixture (*ca.* 17.5 ml. of glacial acetic acid 0.5 *M* in anhydrous sodium acetate) was added. After standing for 24 hr. at 27–29° followed by heating at 45° for 18 hr., the mixture was diluted with 150 ml. of ice–water and extracted three times with ether. The ether extracts were washed with ice–water, twice with cold saturated sodium bicarbonate solution, and again with ice–water. After drying over magnesium sulfate, most of the ether was removed to give 25 ml. of a solution which was cooled in an ice bath and treated with 93 mg. of lithium aluminum hydride. The suspension was allowed to stand at room temperature for 2 days, then was decomposed with 93 μl. of water, 93 μl. of 15% sodium hydroxide solution, and 279 μl. of water with stirring. Magnesium sulfate was added and the solids were removed by filtration. After removal of most of the ether, the residue weighed 203 mg. The weight of products was estimated by analysis on silicone grease at 140° to be 162 mg. Infrared analysis before lithium aluminum hydride reduction showed that little or no tosylate was present.

The products from this and similar solvolyses were separated into alcohol and olefin fractions either by chromatography on alumina (olefins were eluted with 90% pentane–10% ether and alcohols with pure ether) or by gas chromatography (silicone grease at 140–150° or TCEP at 120–140°). Analysis of the olefin mixture on TCEP at 50 or 60° showed two components; the major peak had the retention time of **10** and the minor that of **11**. 3-Methylcyclooctene[4] was excluded as a possible product because there was no peak at its retention time; mixtures of authentic 1-, 3-, and 5-methylcyclooctenes showed three peaks under the

(22) A reaction time of 1.25 hr. was later found to be sufficient, and, in fact, increased the yield slightly, giving **1a** which was 70–75% pure.

(23) A. C. Cope and A. Fournier, *J. Am. Chem. Soc.*, **79**, 3896 (1957).

(24) The tosylate **2a** was unstable at room temperature; therefore no analytical data are reported; however, **2b** was sufficiently stable to survive weighing at room temperature. The disappearance of tosylate in each solvolysis mixture was followed by infrared spectroscopy; **2a** reacted somewhat faster than **2b**.

conditions of the analysis. 4-Methylcyclooctene,[4] which has the same retention time as **10** on TCEP, was eliminated as a possible product when the major component was collected from TCEP and reinjected onto a silver nitrate–tetraethylene glycol column (SNTG) at 76°, conditions known to give marked separation of the 1- and 4-methylcyclooctenes.[4] Only one peak was found, with the retention time of **10**. The olefins **10** (83.4% of the solvolysis mixture) and **11** (9.7% of the solvolysis mixture) were collected (SNTG, 40°) and identified by comparison of their infrared spectra with those of authentic samples. The alcohol fraction was separated into two components on a silicone grease column at 140°. The major component (5.5% of the solvolysis mixture) was identified as **12** and the minor one (0.5% of the solvolysis mixture) as mainly **1b** by comparison of retention times and infrared spectra with those of authentic samples.

Solvolysis of 2b.—Tosylate **2b** (m.p. 42.6–44.0° after two recrystallizations from pentane) was prepared from 222.5 mg. of **1b** and 425 mg. of *p*-toluenesulfonyl chloride in 2 ml. of pyridine in the manner described for the preparation of tosylate **2a**.

Anal. Calcd. for $C_{16}H_{24}O_3S$: C, 64.84; H, 8.16. Found: C, 64.72; H, 8.06.

The tosylate **2b** (280 mg., recrystallized twice from pentane) was solvolyzed immediately in 15 ml. of glacial acetic acid–0.5 *M* sodium acetate for 28 hr. at room temperature, then at 40–45° for 22 hr. The products, obtained in the manner described for the solvolysis of **2a**, weighed 180 mg. and still contained some ether (yield as estimated by gas chromatography on TCEP at 105° was 160 mg.).

The procedure for analysis of the olefin fraction was essentially that described for **2a** except that the major product (11, 74.0%) was first collected on SNTG at 52°, then reinjected on TCEP at 50° to show the absence of both 3- and 4-methylcyclooctene,[4] and collected again for infrared analysis. The minor olefin product (8.2%) was collected on SNTG at 52° for infrared analysis. When solvolysis products were analyzed on TCEP (105°) before lithium aluminum hydride reduction five components, two major and three minor, were found, exclusive of olefins. The two major products, identified by comparison of infrared spectra and retention times with those of authentic samples, were *cis*- (10.1%) and *trans*-5-methylcyclooctyl acetate (4.6%). The minor components were 1-methylcyclooctyl acetate[25] (1.2%) and two unidentified materials (1.0% and 0.9%). The solvolysis products were reduced with lithium aluminum hydride as described previously, separated by gas chromatography (TCEP, 116°), and identified by comparison of retention times and infrared spectra with those of authentic samples as **1** (mainly *cis*) and **12**. The 2-methylcyclooctanols[4] were eliminated as possible products because no peak was found at their retention time. A sample of **1** was collected and oxidized with chromium trioxide–pyridine[4,26] to 5-methylcyclooctanone, identified by its retention time (TCEP, 140°) and infrared spectrum (comparison with that of an authentic sample). Quantitative infrared studies showed that 3-methylcyclooctanone could not have been present in the sample to an amount >10%.[27]

Stability to the Solvolysis Conditions. A. Olefin Products.—One part of olefin (**10** and **11** in separate experiments) and one part of *p*-toluenesulfonic acid monohydrate were treated with about 50 parts of acetic acid–0.5 *M* sodium acetate for 24.5 hr. at 25° and 24 hr. at 45° and worked up as for the solvolyses. The olefins were recovered unchanged (identified by their retention times and infrared spectra) in high yields.

B. Acetate Products.—*cis*- and *trans*-5-methylcyclooctyl acetates were each shown to be stable to the solvolysis conditions as described above. 1-Methylcyclooctyl acetate[16] was not completely stable, decomposing to **10** to the extent of *ca.* 30%. (Identifications were made by retention times and infrared spectra.) In a typical run, 17 mg. of 1-methylcyclooctyl acetate was treated with 17 mg. of *p*-toluenesulfonic acid monohydrate and 0.80 ml. of acetic acid–0.5 *M* sodium acetate for 25.5 hr. at 25° followed by 21 hr. at 45°. The product (15 mg.) was shown to contain 30.5% of 1-methylcyclooctene and 69.5% of 1-methylcyclooctyl acetate by infrared and gas chromatographic (TCEP, 110°) analyses.

C. 5-Methylcyclooctanols.—The alcohols **1a** and **1b** were shown to be acetylated to the extent of 9% [infrared and gas chromatographic analyses (TCEP, 140°)] when treated with acetic acid–0.5 *M* sodium acetate for 25.5 hr. at 25° followed by 22 hr. at 45°.

(25) Identified by retention time only; the acetate was somewhat unstable to gas chromatography.

(26) G. I. Poos, G. E. Arth, R. E. Beyler, and C. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(27) This limits the presence of 3-methylcyclooctanone in the solvolysis products to <2.5%, as the sample of 5-methylcyclooctanone used in this study corresponded to about 25% of the solvolysis mixture.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Proximity Effects. XXXVI. Solvolyses of Deuterium-Labeled Cyclooctyl Brosylate[1,2]

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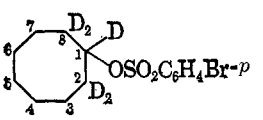
Cyclooctyl brosylate-1,2,2,8,8,-d_5 was solvolyzed in glacial acetic acid–sodium acetate, formic acid–sodium formate, and in trifluoroacetic acid–sodium acetate, and in each case the deuterium distribution in the substitution and elimination products was determined by mass spectrometry. The extents of rearrangement observed were about 53% for the acetolysis, 60% for the formolysis, and >62% for the trifluoroacetolysis. In the first two cases rearrangement proceeded almost exclusively by a transannular 1,5-hydride shift; the extent of 1,3-hydride shift was not appreciable. Conformational and mechanistic implications of the data are discussed.

Solvolysis of deuterium-labeled *cis*-cyclooctene oxide in formic acid has shown that both 1,5- and 1,3-hydride shifts occurred. The 1,5-shift predominated by 61 to 39 in the formation of *cis*-1,4-cyclooctanediol, and by 94 to 6% in the formation of 3-cycloocten-1-ol.[4,5] On the other hand, 1,5-hydride shift took place to the exclusion of 1,3-hydride shift in the acetolysis of 5-methyl- and 5-*t*-butylcyclooctyl tosylates.[6,7] Conformational and electronic effects due to the epoxide ring may be expected to change the nature of the hydride shifts in the case of *cis*-cyclooctene oxide. Likewise, the solvolysis of 5-alkylcyclooctyl tosylates may be influenced by electronic and conformational effects of the alkyl groups.

This paper reports an investigation of the transannular hydride shifts that occur in cyclooctyl brosylate modified only by the deuterium substitution shown in formula **1**.



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(2) Paper XXXV, *J. Am. Chem. Soc.*, **85**, 3743 (1963).

(3) National Institutes of Health Predoctoral Fellow, 1961–1963; National Science Foundation Summer Fellow, 1961.

(4) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *J. Am. Chem. Soc.*, **82**, 6366 (1960).

(5) The possible influence of isotope effects was not considered in arriving at these figures, but would not substantially alter the data. For example, if deuteride should migrate rather than hydride, the maximum probable value for rate decrease is threefold; see C. G. Swain, R. A. Wiles, and R. W. Bader, *J. Am. Chem. Soc.*, **83**, 1945 (1961), and references cited therein. Using this value and assuming equal numbers of deuterium and hydrogen atoms in the 5- and 6-positions with the proper stereochemistry for migration, the corrected percentages of 1,5-hydride shift are 70% for the formation of *cis*-1,4-cyclooctanediol and 96% for the formation of 3-cycloocten-1-ol.

(6) A. C. Cope and D. M. Gale, *J. Am. Chem. Soc.*, **85**, 3743 (1963).

(7) N. L. Allinger and S. Greenberg, *ibid.*, **84**, 2394 (1962).